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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/842,776	04/27/2001	Christian Reiter	41735	4137

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EXAMINER	
NAVARRO, ALBERT MARK	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 04/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/842,776	REITER ET AL.	
	Examiner	Art Unit	
	Mark Navarro	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 54-91 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 54-91 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendment filed February 6, 2004 has been received and entered. Claims 1-4 and 13-14 have been canceled and new claims 54-91 have been added. Consequently, claims 54-91 are pending in the instant application.

Claim Rejections - 35 USC § 112

1. The rejection of claims 1-4 and 13-14 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained as applied to newly added claims 54-91.

The claims are directed to methods for detecting an infection of an acid-resistant microorganism in stool with a monoclonal antibody or "fragment or derivative thereof."

Applicants are asserting that the invention, as claimed in new independent claim 54 is directed to a monoclonal antibody or fragment or derivative thereof which "specifically binds to an epitope of a first antigen" and the second monoclonal antibody or fragment or derivative thereof "specifically binds an epitope of a second antigen." Applicants further assert that not "every" antibody fragment or derivative is claimed, but only those antibodies or fragments or derivatives thereof which "specifically bind to an epitope of a first or second antigen." Applicants conclude that it is evident, that neither a single amino acid nor a combination of CDRs which are not in the proper orientation will bind to the epitope.

Applicants arguments have been fully considered but are not found to be fully persuasive.

First, Applicants assert that the newly filed claims are directed to a monoclonal antibody or fragment or derivative thereof which "specifically binds to an epitope of a first antigen" and the second monoclonal antibody or fragment or derivative thereof "specifically binds an epitope of a second antigen." However, what does the structure of this epitope look like? The claims shed no light on this missing information. Without guidance as to what the structure of the immunogen looks like, one of skill in the art would be hard pressed to determine which antibodies are capable of specifically binding an undisclosed structure. To further complicate this, Applicants claims recite "derivatives" which allow for multiple amino acid substitutions, insertions and deletions within this epitope of undefined structure. As set forth in Rudinger et al "Peptide Hormones" edited by Parsons et al, University Park Press, June 1976, pages 1-7, especially page 6, teach that "the significance of particular amino acids and sequences for different aspects of biological activity cannot be determined a priori but must be determined from case to case by painstaking experimental study."

Second, Applicants further assert that not "every" antibody fragment or derivative is claimed, but only those antibodies or fragments or derivatives thereof which "specifically bind to an epitope of a first or second antigen." However, again what structure is set forth in the claims for this epitope? None. One of skill in the art would be forced into excessive experimentation to determine which antibodies are capable of "specifically" binding to an epitope of undefined structure.

Finally, Applicants conclude that it is evident, that neither a single amino acid nor a combination of CDRs which are not in the proper orientation will bind to the epitope. This statement is exactly the point the Examiner is trying to make. One of skill in the art would be forced into excessive experimentation to identify antibodies which are capable of "specifically binding" an epitope which has no structural limitations on it in the first place.

In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to producing and using the myriad of derivatives encompassed in the scope of the claims one skill in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

For reasons of record, as well as the reasons set forth above, this rejection is maintained.

2. The rejection of claims 1-4 and 13-14 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained as applied to newly added claims 54-91.

The claims are directed to methods for detecting an infection of an acid resistant microorganism in the stool wherein the monoclonal antibody specifically binds an "epitope of the first antigen" and specifically binds "an epitope of a second antigen."

Applicants are asserting that the method of the invention does not require the identity of fragments which are able to mimic secondary or tertiary structures of the full length polypeptide, but only to use the antibodies which bind to epitopes which survive the intestine and are present in the stool. Applicants further assert that Example 6, of the specification, sets forth of a preferred binding assay, and using this assay, it is possible to determine whether a particular peptide fragment contains the epitope, and whether it must necessarily bind the monoclonal antibody.

Applicants arguments have been fully considered but are not found to be fully persuasive.

First, Applicants assert that the method of the invention does not require the identity of fragments which are able to mimic secondary or tertiary structures of the full length polypeptide, but only to use the antibodies which bind to epitopes which survive the intestine and are present in the stool. However, Applicants are respectfully directed to the claim language which recites "an **epitope** of an antigen." (Emphasis added). This is directly addressed by the teachings of Fox (US Patent Number 4,879,213), which sets forth that "short linear polypeptides often appear not to have the ability to mimic the required secondary and tertiary conformational structures to constitute appropriate immunogenic and antigenic determinants." (See column 3). This is directly analogous to Applicants claim to an "epitope" of an antigen. An epitope is a short linear peptide obtained from a larger antigenic structure which has secondary and tertiary conformational structures.

Finally, Applicants assert that Example 6 sets forth of a preferred binding assay, and using this assay, it is possible to determine whether a particular peptide fragment contains the epitope, and whether it must necessarily bind the monoclonal antibody. However, returning to the claims, one of skill in the art is not in possession of a structure to use in the preferred binding assay in the first place. Further trying to determine which epitope of the undefined structure is referred to would require excessive experimentation.

For reasons of record, as well as the reasons set forth above, this rejection is maintained.

3. The rejection of claims 1-4 and 13-14 under 35 U.S.C. 112, second paragraph, as being indefinite vague and indefinite in the recitation of "derivative" is maintained as applied to newly submitted claims 54-91.

Applicants are asserting that this phrase is not unclear, but rather well defined, and methods for obtaining derivatives are adequately disclosed in the specification.

Applicants arguments have been fully considered but are not found to be persuasive.

Applicants arguments are not found to be persuasive in view of the term "derivative." Derivative as defined by Dorlands Medical Dictionary 27th Edition, 1988 is a substance derived from another substance "either directly or by modification." The degree the substance can be modified and still remain under the scope of a derivative, simply cannot be determined by one of skill in the art.

For reasons of record, as well as the reasons set forth above, this rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. The rejection of claims 1-4 under 35 U.S.C. 102(b) as being anticipated by Larka et al as applied to newly submitted claims 54-57, 74 and 76 is maintained.

Applicants are asserting that the present application claims priority to PCT/EP99/08212 filed October 29, 1999, and EP 98 120687.3 filed November 6, 1998 and EP 98 120517.2 filed October 29, 1998, and that Larka published in 1999 is not a proper reference under 35 USC 102(b). Applicants further assert that Larka unambiguously states that problems relating to cross-reactivity and strain variation with immunoassays for detection of H. pylori "rule out the use of monoclonal antibodies." Applicants further assert that it is the use of at least two different antigens that provides for the increased reliability offered by the method of the claimed invention.

Applicants arguments have been fully considered but are not found to be fully persuasive.

First, Applicants are asserting that the present application claims priority to PCT/EP99/08212 filed October 29, 1999, and EP 98 120687.3 filed November 6, 1998 and EP 98 120517.2 filed October 29, 1998, and that Larka published in 1999 is not a proper reference under 35 USC 102(b). However as set forth by the MPEP, to properly claim benefit of priority of an earlier application, Applicants must either make reference to the applications in the first line of the specification, or alternatively list the priority within an Application Data Sheet. In view that Applicant has not complied with either of these requirements, priority has not be given.

For original applications filed under 35 U.S.C. 111(a) (other than a design application) on or after November 29, 2000, the time period is during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior foreign application. For applications that have entered national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the claim for priority must be made during the pendency of the application and within the time limit set forth in the PCT and the Regulations under the PCT. See 37 CFR 1.55(a)(1)(ii). If applicant desires priority under 35 U.S.C. 119(a)-(d), (f) or 365(a) based upon a prior foreign application, applicant must file a petition for an unintentionally delayed priority claim (37 CFR 1.55(c)). The petition must be accompanied by (1) the claim (i.e., the claim required by 35 U.S.C. 119(a)-(d) and (f) and 37 CFR 1.55) for priority to the prior foreign application, unless previously submitted; (2) a surcharge under 37 CFR 1.17(t); and (3) a statement that the entire delay between the date the claim was due under 37 CFR

1.55(a)(1) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Second, Applicants assert that Larka unambiguously states that problems relating to cross-reactivity and strain variation with immunoassays for detection of H. pylori "rule out the use of monoclonal antibodies." However, Applicants are quoting from the background of the invention. Applicants are directed to the summary of the invention (Column 2, lines 46-50) which set forth that "those skilled in the art will also recognize that two or more monoclonal antibodies could be used as an alternative to using polyclonal antibodies."

Finally, Applicants assert that it is the use of at least two different antigens that provides for the increased reliability offered by the method of the claimed invention. However, Applicants are respectfully directed back to the claims. The claims recite "epitope of a second antigen, differing from the epitope of the first antigen." However, there is no requirement that the antigens must be different as argued by Applicants. Simply stated, two different epitopes on the same antigen are encompassed. Consequently, the disclosure of Larka et al is deemed to anticipate the instantly filed claims.

For reasons of record, as well as the reasons set forth above, this rejection is maintained.

The following new grounds of rejection are applied:

Claim Rejections - 35 USC § 112

2. Claims 64, 67, 73, 80, 83 & 87 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is objected to under 35 U.S.C. 112, first paragraph, as failing to provide an enabling disclosure without complete evidence that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of biological materials.

The specification lacks complete deposit information for the deposit of DSM ACC2362, DSM ACC2356, DSM ACC2355, DSM ACC2362. It is not clear that strains possessing the identical properties of DSM ACC2362, DSM ACC2356, DSM ACC2355, DSM ACC2362 are known and publicly available or can be reproducibly isolated from nature without undue experimentation.

Exact replication of a cell line is an unpredictable event. Although applicant has provided a written description of a method for selecting the claimed cell line, this method will not necessarily reproduce strains which are chemically and structurally identical to those claimed. Undue experimentation would be required to screen all of the possible strain species to obtain the claimed strain.

Because one skilled in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the DSM ACC2362, DSM ACC2356, DSM ACC2355, DSM ACC2362, a suitable deposit for patent purposes, evidence of public availability of the DSM ACC2362, DSM ACC2356, DSM ACC2355, DSM ACC2362 or evidence of the reproducibility without undue experimentation is required.

If the deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has

authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of deposit and the complete name and full street address of the depository is required. As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposits have not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

In addition, a deposit of biological material that is capable of self-replication either directly or indirectly must be viable at the time of deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1) The name and address of the depository;
2) The name and address of the depositor;
3) The date of deposit;
4) The identity of the deposit and the accession number given by the depository;
5) The date of the viability test;
6) The procedures used to obtain a sample if the test is not done by the depository; and
7) A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the cell line described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundack, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro whose telephone number is (571) 272-0861. If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark Navarro
Primary Examiner
April 16, 2004